

Arterial and venous endothelial cells are molecularly distinct from the earliest stages of angiogenesis. This distinction is revealed by expression on arterial cells of a transmembrane ligand, called EphrinB2 whose receptor EphB4 is expressed on venous cells. Targeted disruption of the *EphrinB2* gene prevents the remodeling of veins from a capillary plexus into properly branched structures. Moreover, it also disrupts the remodeling of arteries, suggesting that reciprocal interactions between pre-specified arterial and venous endothelial cells are necessary for angiogenesis. This distinction can be used to advantage in methods to alter angiogenesis, methods to assess the effect of drugs on artery cells and vein cells, and methods to identify and isolate artery cells and vein cells, for example.